

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF MISSOURI
EASTERN DIVISION

IN RE NUVARING® PRODUCTS)
LIABILITY LITIGATION)
)

Case No. 4:08-MD-1964 RWS

MARIANNE PRATHER,)
)
 Plaintiff)

v.)

Case No. 4:08-cv-00558-RWS

ORGANON USA, INC. *et al.*)
)
 Defendants.)

MEMORANDUM AND ORDER

Defendants in this matter (hereinafter “Organon”) bring a Daubert motion to exclude testimony from Dr. John Richart. Specifically, Organon asks me to bar Dr. Richart’s opinion that the plaintiff, Marianne Prather (“Prather”) would not have suffered a pulmonary embolism had she not used NuvaRing. By bringing this motion, Organon asks me to find, as a matter of law, that Dr. Richart’s opinion is so unreliable that it should be excluded from being tested by any cross-examination at trial, being weighed by any jury, or even limited in any respect by any trial judge. After reading the voluminous briefs and exhibits filed by both sides on this issue, I am not persuaded that Dr. Richart’s opinion that Prather would not have suffered a pulmonary embolism is unreliable. I will deny Organon’s motion to exclude Dr. Richart’s proffered testimony.

I. BACKGROUND

NuvaRing, which is manufactured, marketed, and sold by Organon, is a member of a class of prescription drugs known as combined hormonal contraceptives (“CHCs”). Unlike oral CHCs, NuvaRing takes the form of a flexible ring which releases hormones over the course of treatment. The ring is vaginally inserted by women for birth control. Each month, the ring is removed and a new ring is inserted.

CHCs contain an estrogen, typically ethinyl estradiol (“EE”), and a progestin. The “generation” of CHC depends upon the type of progestin. Each “generation” of CHC typically uses the following progestins: first-generation contains norethynodrel; second-generation contains levonorgestrel; and third-generation CHCs contain desogestrel, gestodene, or norgestimate. NuvaRing uses the active metabolite of desogestrel, etonogestrel, and is therefore considered a third-generation progestin.

All CHCs can cause venous thromboembolism (“VTE”), including deep vein thrombosis (“DVT”) and pulmonary embolism.¹ (Doc. 28, Organon Mem. Supp.). First-generation CHCs use high levels of EE and are associated with high incidence rates of VTE. Second-generation CHCs use a reduced amount of EE and are associated with less risk for VTE. It is generally accepted that risk of thrombosis is correlated with estrogen dose.

Third-generation CHCs use lower amounts of estrogen than prior generations; however, some studies have found an increased risk for VTE with some third-generation oral CHCs as compared to second-generation oral CHCs. Prather claims that the third-generation progestin used in NuvaRing, etonogestrel, has been linked to undisclosed higher risk for VTE, including

¹ Venous thromboembolism is a blood clot that forms within a vein. Deep vein thrombosis is a blood clot that forms in a vein not externally visible, typically in the veins of the lower extremities. A pulmonary embolism forms when part or all of a blood clot breaks free and lodges in one of the lungs. These conditions have varying severity and can be life threatening.

both DVT and pulmonary embolism. Prather also contends that NuvaRing's use results in occasional bursts of estrogen that are unopposed by progestin and that this increases the prothrombotic propensities of NuvaRing.

Prather has been on and off oral contraceptives since age eighteen. From 1992 through 1994, Prather used first- and third-generation oral CHCs. She had her first child in 1997 and began using Desogen, a third-generation CHC, until 1998, when she ceased using hormonal birth control. In 2002, Prather had her second child. From 1998 until August 2003, Prather used condoms as her primary method of contraception.

Prather was prescribed and began using NuvaRing in late August 2003. At the end of September 2003, Prather began to experience leg discomfort and shortness of breath. On October 4, 2003, Prather visited the emergency room, where an ultrasound revealed a deep vein thrombosis in her left leg, and a CT scan revealed multiple pulmonary emboli.

In support of her claims, Prather offers testimony from Dr. John Richart, a hematologist. Dr. Richart will testify that NuvaRing is a substantial contributing cause of Prather's pulmonary embolism. Dr. Richart also opines that Prather would not have suffered a pulmonary embolism had she not used the NuvaRing contraceptive. In this motion, Organon only challenges the latter opinion. Organon argues that Dr. Richart's methodology is so unreliable that I should exclude his testimony that Prather's pulmonary embolism would not have occurred had she not used NuvaRing.

II. LEGAL STANDARD

Federal Rule of Evidence 702 and Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579 (1993), govern the admissibility of expert testimony. The Daubert standard applies to all expert

testimony, whether based on scientific competence or other specialized or technical expertise.

See Polski v. Quigley Corp., 538 F.3d 836, 838 (8th Cir. 2008). Rule 702 provides:

If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

“[I]t is the responsibility of the trial judge to determine whether a particular expert has sufficient specialized knowledge to assist jurors in deciding the specific issues in the case.”

Wheeling Pittsburgh Steel Corp. v. Beelman River Terminals, Inc., 254 F.3d 706, 715

(8th Cir. 2001). “Once initial expert qualifications and usefulness to the jury are established, however, a district court must continue to perform its gatekeeping role by ensuring that the actual testimony does not exceed the scope of the expert’s expertise, which if not done can render expert testimony unreliable” Id.

“When faced with a proffer of expert scientific testimony, the trial court must make ‘a preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and of whether that reasoning or methodology properly can be applied to the facts in issue.’” Polski, 538 F.3d at 838 (quoting Daubert, 509 U.S. at 592–93). Thus, under Rule 702, the trial judge also acts as a gatekeeper by screening evidence for relevance and reliability. Daubert, 509 U.S. at 589.

Thus, the district court applies a three-part test when screening expert testimony under Rule 702:

First, evidence based on scientific, technical, or other specialized knowledge must be useful to the finder of fact in deciding the ultimate issue of fact. This is the basic rule of relevancy. Second, the proposed witness must be qualified to assist the finder of fact. Third, the proposed evidence must be reliable or trustworthy in

an evidentiary sense, so that, if the finder of fact accepts it as true, it provides the assistance the finder of fact requires.

Polski, 538 F.3d at 839 (quoting Lauzon v. Senco Prods., Inc., 270 F.3d 681, 686 (8th Cir. 2001)).

“Rule 702 reflects an attempt to liberalize the rules governing the admission of expert testimony. The rule clearly is one of admissibility rather than exclusion.” Lauzon, 270 F.3d at 686 (internal quotations and citations omitted). “The exclusion of an expert’s opinion is proper only if it is so fundamentally unsupported that it can offer no assistance to the jury.” Wood v. Minn. Mining & Mfg. Co., 112 F.3d 306, 309 (8th Cir. 1997) (internal quotations and citation omitted).

When assessing the reliability of expert testimony, a trial court should consider several factors, including: “(1) whether the concept has been tested, (2) whether the concept has been subject to peer review, (3) what the known rate of error is, and (4) whether the concept is generally accepted by the community.” Miller v. Baker Implement Co., 439 F.3d 407, 412 (8th Cir. 2006) (citing Daubert, 509 U.S. at 593–95). There is no requirement that courts rely on each factor, as the gatekeeping inquiry is flexible and must be “tied to the facts” of the particular case. Kumho Tire Co., Ltd. v. Carmichael, 526 U.S. 137, 150 (1999) (quoting Daubert, 509 U.S. at 591).

“[T]he rejection of expert testimony is the exception rather than the rule.” Robinson v. GEICO General Ins. Co., 447 F.3d 1096, 1100 (8th Cir. 2006) (citing Fed. R. Evid. 702 advisory comm. note). “Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence.” Daubert, 509 U.S. at 595.

III. ANALYSIS

A. Dr. Richart's Methodology

Dr. Richart opines that Prather would not have suffered a pulmonary embolism had she not used the NuvaRing. Organon argues that two statements by Dr. Richart demonstrate that Dr. Richart adopted a new methodology after his opinion was challenged and that I should, therefore, reject Dr. Richart's methodology as untimely. Dr. Richart initially stated that "[t]he six years leading up to Ms. Prather's pulmonary embolism can be viewed as a single-patient crossover design trial comparing sequential thrombotic challenges in which Ms. Prather serves as her own control." (Doc. 37-2, Richart Case-Specific Report, at 14). After Organon brought this Daubert motion, Richart stated that he used the process of differential diagnosis, in which he "considered and eliminated all likely causes of Ms. Prather's injury until the most likely cause was isolated" in reaching his medical causation opinion. (Doc. 37-1, Richart Affidavit, at ¶ 8).

A physician performs a differential diagnosis by first "ruling in" all scientifically plausible causes of the plaintiff's injury. The physician then "rules out" the least plausible causes of injury until the most likely cause remains. The final result of a differential diagnosis is the expert's conclusion as to whether the defendant's product caused the plaintiff's injury. See Glastetter v. Novartis Pharm. Corp., 252 F.3d 986, 989 (8th Cir. 2001) (citing Westberry v. Gislaved Gummi AB, 178 F.3d 257, 262–66 (4th Cir. 1999)).

I find that Dr. Richart conducted a differential diagnosis. Dr. Richart relied upon his own expertise as a hematologist, the relevant medical literature, and Prather's medical records to determine a number of potential causes of Prather's DVT. These causes include genetic mutations, advanced age, obesity, childbirth, prolonged immobilization, and the use of CHCs. Dr. Richart eliminated obesity and age as causal agents. (Doc. 37-3, Richart Nov. Dep. at 216 &

243). Dr. Richart disregarded childbirth and prolonged immobilization as Prather's medical records did not include either condition during the relevant time period. Dr. Richart also ruled out prior use of CHCs, as Prather had ceased using hormonal contraceptives prior to her most recent childbirth, and the risk associated with CHCs ended after the hormones "washed out" of her body. (Doc. 37-3 at 196–97; Doc. 37-2 at 15).

Prather's genetic testing revealed two mutations that could potentially increase the risk for blood clots: prothrombin gene mutation and MTHFR mutation. Dr. Richart was able to eliminate MTHFR as a potential cause because the mutation itself is not a risk factor for VTE; rather, MTHFR mutation can lead to elevated homocysteine levels which, in turn, present a weak risk for venous blood clots. Because Prather's blood tests revealed normal levels of homocysteine, MTHFR did not present an increased blood clot risk. (Doc. 37-2 at 11; Doc. 37-3 at 186–87).

It was in ruling out the prothrombin gene mutation that Dr. Richart used the term "single patient, cross-over design trial." Dr. Richart noted that most DVTs are caused by "provoking events" or "challenges." Prather's prothrombin mutation existed during a number of past challenges, including some that presented greater risk for VTE than hormonal contraceptive use,² but never yielded a DVT. Dr. Richart, therefore, concluded that the prothrombin mutation likely did not cause Prather's DVT. (Doc. 37-2 at 14–15).

Dr. Richart's differential diagnosis resulted in only one remaining cause for Prather's DVT: NuvaRing. His conclusion that NuvaRing caused Prather's DVT is bolstered by numerous

² Pregnancy is "the most thrombophilic state in normal human physiology" and carries a fourfold increase in the risk of thromboembolism compared to the non-pregnant population. (Doc. 37-2, "Richart Case-Specific Report" at 14). In addition to her two vaginal births, Prather underwent surgery for "bucket handle tear" of the medial meniscus in September 1987. This surgery required 12 hours of immobilization post-operatively. (*Id.* at 13).

epidemiological studies on third-generation CHCs that link the class of drugs to VTEs as well as by Organon's own clinical trials of NuvaRing during which patients experienced VTEs.³

Though he may not have used the term "differential diagnosis" in his expert report when ruling in and ruling out potential causes, I find that Dr. Richart conducted a differential diagnosis and did not, as Organon argues, adopt the method in response to this Daubert motion. I will not strike Dr. Richart's methodology for untimeliness.

B. Reliability

Organon next argues that Dr. Richart's differential diagnosis lacks sufficient reliability to be admitted at trial. Differential diagnoses are presumptively admissible. Glastetter, 252 F.3d at 989 (citing Turner v. Iowa Fire Equip. Co., 229 F.3d 1202, 1208 (8th Cir. 2000)). Only diagnoses that are scientifically invalid may be excluded. See id. Organon asserts that Dr. Richart's causation opinion is based on two unscientific factors: case reports and temporal proximity.

Organon argues that case reports are incapable of showing causation and, therefore, Dr. Richart's differential diagnosis is unreliable. Case reports, in the absence of other evidence, have been held to be incapable of proving *general* causation.⁴ See In re Baycol Prods. Litig., MDL No. 1431, 2008 WL 6259241, at *17 (D. Minn. Sept. 9, 2008) (citing Siharath v. Sandoz Pharms. Corp., 131 F. Supp. 2d 1347, 1361–62 (N.D. Ga. 2001)). Case reports are useful,

³ Dr. Richart includes in his affidavit citations to an additional epidemiological study that links NuvaRing specifically to an increased risk of VTE. (Doc. 37-2 ¶ 10). While Dr. Richart could not rely upon this study at the time he formed his opinion, I find that it provides additional support for his opinion that NuvaRing caused Prather's DVT.

⁴ General causation is a showing that the drug or chemical is capable of causing the type of harm from which the plaintiff suffers. Junk v. Terminix Int'l Co., 628 F.3d 439, 450 (8th Cir. 2010).

however, in proving *specific* causation.⁵ Siharath, 131 F. Supp. 2d at 1363; see also In re Baycol, 2008 WL 6259241, at *17 (“[Case reports] may rule out other potential causes of the effect”) (citing Rider v. Sandoz Pharms. Corp., 295 F.3d 1194, 1199 (11th Cir. 2004)); Hardyman v. Norfolk & W. Ry. Co., 243 F.3d 255, 260 (6th Cir. 2001) (“The physician . . . eliminates alternative causes based on a physical examination, clinical tests, and a thorough case history.”) (alteration in original) (quoting Federal Judicial Center, Reference Manual on Scientific Evidence 214 (1994)). Dr. Richart’s use of a case report does not render his differential diagnosis unreliable.

Organon next argues that the temporal relationship between Prather’s NuvaRing use and the onset of her DVT and pulmonary embolism cannot be used to show that the NuvaRing caused those conditions. Contrary to Organon’s arguments, the Eighth Circuit continues to recognize temporal proximity as evidence of causation. See Bland v. Verizon Wireless, (VAW) LLC, 538 F.3d 893, 398 (8th Cir. 2008). It is “in the absence of an established scientific connection between exposure and illness” that temporal connections receive little weight. Id. at 898–99 (citing Moore v. Ashland Chem., Inc., 151 F.3d 269, 278 (5th Cir. 1998)). Dr. Richart is not using temporal proximity to show that NuvaRing is *capable* of causing DVT or pulmonary embolism. Nor is he using temporal proximity to exclude other CHCs from being capable of causing those conditions. Rather, Dr. Richart used temporal proximity to show that NuvaRing did, in fact, cause Prather’s DVT and pulmonary emboli—that, unlike other CHCs Prather had used and that had “washed out” of her system, NuvaRing still presented an ongoing causative link. This is a permissible use of temporal proximity.

⁵ Specific causation is evidence that the drug or chemical in fact caused the harm from which the plaintiff suffers. Junk, 628 F.3d at 450.

In its memoranda in support of this motion, Organon repeatedly frames Dr. Richart's opinion as being that Prather would have avoided a VTE "if she had stayed on Desogen." However, Organon builds a straw-man opinion that goes beyond Dr. Richart's actual opinion. Dr. Richart concludes, simply, that but for her use of NuvaRing, Prather would not have suffered a pulmonary embolism.

In any case, Dr. Richart is not obliged to rule out every conceivable cause in order to present testimony that NuvaRing was the cause in fact of Prather's pulmonary embolism. "An 'expert's causation conclusion should not be excluded because he or she has failed to rule out every possible alternative cause.'" Lauzon v. Senco Products, Inc., 270 F.3d 681, 693 (8th Cir. 2001) (quoting Westberry v. Gislaved Gummi AB, 178 F.3d 257, 265 (4th Cir. 1999)); accord Heller v. Shaw Indus., Inc., 167 F.3d 146, 156 (3rd Cir. 1999)). "The alternative causes suggested by a defendant 'affect the weight that the jury should give the expert's testimony and not the admissibility of that testimony,' unless the expert can offer '*no* explanation for why she has concluded [an alternative cause offered by the opposing party] was not the sole cause.'" Westberry, 178 F.3d at 265 (alteration in original) (citations omitted) (quoting Heller, 167 F.3d at 156–57); see also Lauzon, 270 F.3d at 694 (holding expert's testimony allowing for other potential causes of accident does not preclude causation testimony).

Dr. Richart testified that, although it was "possible" that Prather would have suffered a VTE had she been on a third-generation or second-generation oral CHC, it was "improbable." (Doc. 37-3 at 256 & 264). He based this reasoning on temporal proximity and the fact that Prather had undergone many thrombotic challenges and had already taken Desogen and a first-generation CHC without incident. Because Dr. Richart has provided *some* explanation for his conclusion, it is admissible.

C. Qualifications and Helpfulness to the Finder of Fact

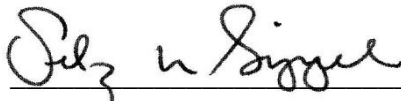
Dr. Richart is a certified hematologist with twelve years of clinical experience in the management of bleeding and thrombotic disorders. He is an Associate Professor of Medicine in the Division of Hematology and Oncology of the Saint Louis University School of Medicine. I find Dr. Richart qualified to testify as an expert on the cause of Prather's pulmonary embolism. Moreover, this subject involves complicated subject matter that is outside of the normal understanding of the layperson. I find that Dr. Richart's testimony will assist the jury.

IV. CONCLUSION

For the foregoing reasons, I find Dr. Richart qualified to opine as to the matters stated in his case-specific expert report. I find that Dr. Richart conducted a differential diagnosis in reaching his opinions that NuvaRing is a substantial contributing factor for Prather's pulmonary embolism and that, but for her use of NuvaRing, Prather would not have suffered the pulmonary embolism. I further find that Dr. Richart's causation opinions, as grounded in credible articles, studies, reports, and personal experience, are based on a reliable methodology and shall be helpful to the finder of fact.

Accordingly,

IT IS HEREBY ORDERED that Organon's motion to exclude the expert testimony of Dr. Richart (Doc. 27) is **DENIED**.



RODNEY W. SIPPEL
UNITED STATES DISTRICT JUDGE

Dated this 10th day of April, 2013.